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*Admitted only in Maryland
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•Practice Limited to
Federal Agencies

June 10, 2004

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Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Art Unit 1614

Re: U.S. Utility Patent Application
Application No. 10/643,226; Filed: August 19, 2003
For: **Method of Screening for Drugs Useful in Treating Alzheimer's Disease**
Inventors: **Bush et al.**
Our Ref: 0609.4810002/TJS/FRC

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Information Disclosure Statement;
2. A listing of the cited documents on form PTO-1449 (70 sheets); and
3. Return postcard.

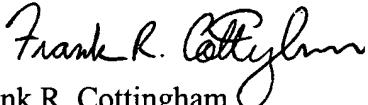
It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

Commissioner for Patents
June 10, 2004
Page 2

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.


Frank R. Cottingham
Attorney for Applicants
Registration No. 50,437

FRC/pcd
Encls.

274391v1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



In re application of:

BUSH *et al.*

Appl. No. 10/643,226

Filed: August 19, 2003

For: **Method of Screening for Drugs
Useful in Treating Alzheimer's
Disease**

Confirmation No.: 3164

Art Unit: 1614

Examiner: *To be assigned*

Atty. Docket: 0609.4810002/TJS/FRC

Information Disclosure Statement

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated. Applicants would like to direct the Examiner's attention to documents AS1, AT4, AS9, AT9, AS10, AT11, AT36, and AR44, for which the month of publication could not be determined after reasonable and diligent efforts to do so.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

In accordance with 37 C.F.R. § 1.98(a)(3), Applicants' undersigned representative submits the following in regards to non-English language document AL4 cited on Form PTO-1449:

Document AL4, German Patent No. DE 40 04 978 A1 is in the German language. An English language abstract of document AL4 was submitted as document AR69.

Copies of documents AG2, AH2, and AI2 are not provided in accordance with the U.S. Patent and Trademark Office pre-OG notice of July 11, 2003, which states "[t]he Office hereby waives the requirement under 37 CFR 1.98 (a)(2)(i) for submitting a copy of each cited U.S. patent and each U.S. patent application publication for all U.S. national patent applications filed after June 30, 2003."

Copies of all other documents were cited by or submitted to the Office in an IDS that complies with 37 C.F.R. § 1.98(a)-(c) in Application No. 09/560,883, filed April 28, 2000, or in Application No. 09/380,704, filed September 8, 1999, or in Application No.

08/816,122, filed March 11, 1997, which are relied upon for an earlier filing date under 35 U.S.C. § 120. Thus, copies of these documents are not attached. 37 C.F.R. § 1.98(d).

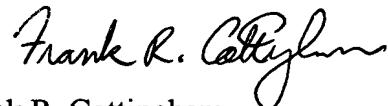
This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Frank R. Cottingham
Attorney for Applicants
Registration No. 50,437

Date: June 10, 2007

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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT 		ATTY. DOCKET NO. 0609.4810002/TJS/FRC		APPLICATION NO. 10/643,226	
		APPLICANT Bush et al.			
		FILING DATE August 19, 2003		GROUP 1614	

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA1	5,242,932	09/07/1993	Gandy et al.			12/17/1991
	AB1	5,373,021	12/13/1994	Marangos			04/26/1993
	AC1	5,357,636	10/25/1994	Dresdner, Jr. et al.			06/30/1992
	AD1	5,523,295	06/04/1996	Fasman			07/06/1994
	AE1	5,688,516	11/18/1997	Raad et al.			10/03/1994
	AF1	5,688,651	11/18/1997	Solomon			12/16/1994
	AG1	5,705,401	01/06/1998	Masters et al.			09/16/1994
	AH1	5,707,821	01/13/1998	Rydel et al.			06/07/1995
	AI1	5,721,106	02/24/1998	Maggio et al.			09/12/1994
	AJ1	5,927,283	07/27/1999	Abraham et al.			05/08/1997
	AK1	5,110,493	05/05/1992	Cherng-Chyi et al.			12/07/1990

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL1	WO 92/18111	10/29/1992	WIPO			Yes No
	AM1	WO 93/10459	05/27/1993	WIPO			Yes No
	AN1	WO 93/24451	12/09/1993	WIPO			Yes No
	AO1	WO 94/04167	03/03/1994	WIPO			Yes No
	AP1	WO 95/31199	11/23/1995	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	1	Assaf, S.Y., and Chung, S.-H., "Release of endogenous Zn ²⁺ from brain tissue during activity," <i>Nature</i> 308:734-736, Nature Publishing Co. (1984).
AS	1	Atwood, C.S., et al., "Copper-Mediated Aggregation and Polymerization of A β ," <i>Soc. Neurosci. Abstr.</i> 23:1883, Society for Neuroscience (1997).
AT	1	Atwood, C.S., et al., "Dramatic aggregation of Alzheimer abeta by Cu(II) is induced by conditions representing physiological acidosis," <i>J. Biol. Chem.</i> 273:12817-12826, American Society for Biochemistry and Molecular Biology (May 1998).

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

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U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA2	5,466,680	11/14/1995	Rudy			03/26/1992
	AB2	6,001,852	12/14/1999	Gerolymatos			02/13/1998
	AC2	5,994,323	11/30/1999	Gerolymatos			02/13/1998
	AD2	5,980,914	11/09/1999	Gerolymatos			02/13/1998
	AE2	4,419,365	12/06/1983	McLachlan, D.R.			12/21/1981
	AF2	5,310,936	05/10/1994	Regtop et al.			01/15/1992
	AG2	2002/0025944 A1	02/28/2002	Bush et al.			10/10/2001
	AH2	2002/0082273 A1	06/27/2002	Bush et al.			09/21/2001
	AI2	6,323,218 B1	11/27/2001	Bush et al.			03/11/1998
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL2	WO 96/07096	03/07/1996	WIPO			Yes No
	AM2	WO 96/12544	05/02/1996	WIPO			Yes No
	AN2	WO 96/28471	09/19/1996	WIPO			Yes No
	AO2	WO 97/04794	02/13/1997	WIPO			Yes No
	AP2	WO 97/09976	03/20/1997	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	2	Bacon, P.A., et al., "Rheumatoid Disease, Amyloidosis and its Treatment with Penicillamine," <i>Eur. J. Rheum. Inflamm.</i> 2:70-74, Cameron Publishers (1979).
AS	2	Barrow, C.J., and Zagorski, M.G., "Solution Structures of β Peptide and Its Constituent Fragments: Relation to Amyloid Deposition," <i>Science</i> 253:179-182, American Association for the Advancement of Science (1991).
AT	2	Barrow, C.J., et al., "Solution Conformations and Aggregational Properties of Synthetic Amyloid β -Peptides of Alzheimer's Disease," <i>J. Mol. Biol.</i> 225:1075-1093, Academic Press (1992).

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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL3	WO 97/36885	10/09/1997	WIPO			Yes No
	AM3	WO 98/06403	02/19/1998	WIPO			Yes No
	AN3	WO 98/40071	09/17/1998	WIPO			Yes No
	AO3	WO 99/09981	03/04/1999	WIPO			Yes No
	AP3	WO 99/18432	04/15/1999	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	3	Basun, H., et al., "Metals and trace elements in plasma and cerebrospinal fluid in normal aging and Alzheimer's disease," <i>J. Neural Transm. [P-D Sect.]</i> 3:231-258, Springer-Verlag (1991).
AS	3	Beal, M. F., "Energy, Oxidative Damage, and Alzheimer's Disease: Clues to the Underlying Puzzle," <i>Neurobiol. Aging</i> 15:S171-S174, Pergamon Press (1994).
AT	3	Behl, C., et al., "Hydrogen Peroxide Mediates Amyloid β Protein Toxicity," <i>Cell</i> 77:817-827, Cell Press (1994).

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL4	DE 40 04 978 A1	08/22/1991	Germany			Yes X No
	AM4	WO 94/27594	12/08/1994	WIPO			Yes No
	AN4	WO 96/39144	12/12/1996	WIPO			Yes No
	AO4	WO 97/01559	01/16/1997	WIPO			Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	4	Biaglow, J.E., and Kachur, A.V., "The Generation of Hydroxyl Radicals in the Reaction of Molecular Oxygen with Polyphosphate Complexes of Ferrous Ion," <i>Radiation Res.</i> 148:181-187, Kluge Carden Jennings Pub. Co. (August 1997).
AS	4	Boado, R.J., et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of Alzheimer's Disease and Cerebral AIDS," <i>J. Pharm. Sci.</i> 87(11):1308-1315, American Pharmaceutical Association (November 1998).
AT	4	Borman, S., "Diverse Strategies Emerge For Diagnosing Alzheimer's Disease," <i>Chem. Eng. News</i> 272:33-34, American Chemical Society (1996).

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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	5	Brown, D.R., et al., "Normal prion protein has an activity like that of superoxide dismutase," <i>Biochem. J.</i> 344:1-5, Biochemical Society/Portland Press (November 1999).
AS	5	Bruce, A.J., et al., " β -Amyloid toxicity in organotypic hippocampal cultures: Protection by EUK-8, a synthetic catalytic free radical scavenger," <i>Proc. Natl. Acad. Sci. USA</i> 93:2312-2316, National Academy of Sciences (March 1996).
AT	5	Bruijn, L.I., et al., "ALS-Linked SOD1 Mutant G85R Mediates Damage to Astrocytes and Promotes Rapidly Progressive Disease with SOD1-Containing Inclusions," <i>Neuron</i> 18:327-338, Cell Press (February 1997).

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	AL						Yes No
	AM						Yes No
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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	6	Burdick, D., et al., "Assembly and Aggregation Properties of Synthetic Alzheimer's A4/β Amyloid Peptide Analogs," <i>J. Biol. Chem.</i> 267:546-554, American Society for Biochemistry and Molecular Biology (1992).
AS	6	Burns, J.A., et al., "Selective Reduction of Disulfides by Tris(2-carboxyethyl)phosphine," <i>J. Org. Chem.</i> 56:2648-2650, American Chemical Society (1991).
AT	6	Busciglio, J., and Yankner, B.A., "Apoptosis and increased generation of reactive oxygen species in Down's Syndrome neurons <i>in vitro</i> ," <i>Nature</i> 378:776-779, Nature Publishing Co. (1995).

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	AM						Yes No
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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	7	Bush, A.I., et al., "A Novel Zinc(II) Binding Site Modulates the Function of the β A4 Amyloid Protein Precursor of Alzheimer's Disease," <i>J. Biol. Chem.</i> 268:16109-16112, American Society for Biochemistry and Molecular Biology (1993).
AS	7	Bush, A.I., et al., "Alzheimer A β functions as a superoxide antioxidant <i>in vitro</i> and <i>in vivo</i> ," <i>Soc. Neurosci. Abstr.</i> 25:14, Society for Neuroscience (October 1999).
AT	7	Bush, A.I., et al., "Modulation of A β Adhesiveness and Secretase Site Cleavage by Zinc," <i>J. Biol. Chem.</i> 269:12152-12158, American Society for Biochemistry and Molecular Biology (1994).

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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	8	Bush, A.I., et al., "The Amyloid β -Protein Precursor and Its Mammalian Homologues," <i>J. Biol. Chem.</i> 269:26618-26621, American Society for Biochemistry and Molecular Biology (1994).
AS	8	Bush, A.I., et al., "Rapid Induction of Alzheimer A β Amyloid Formation by Zinc," <i>Science</i> 265:1464-1467, American Association for the Advancement of Science (1994).
AT	8	Bush, A.I., et al., "Response to Zinc and Alzheimer's Disease," <i>Science</i> 268:1920-1923, American Association for the Advancement of Science (1995).

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	AO						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	9	Butterfield, D.A., et al., "β-Amyloid Peptide Free Radical Fragments Initiate Synaptosomal Lipoperoxidation in a Sequence-Specific Fashion: Implications to Alzheimer's Disease," <i>Biochem. Biophys. Res. Commun.</i> 200:710-715, Academic Press (1994).
AS	9	Butterfield, D.A., et al., "Aβ(25-35) Peptide Displays H ₂ O ₂ -Like Reactivity Towards Aqueous Fe ²⁺ , Nitroxide Spin Probes, and Synaptosomal Membrane Proteins," <i>Life Sci.</i> 58:217-228, Pergamon Press (1996).
AT	9	Ceballos-Picot, I., et al., "Peripheral Antioxidant Enzyme Activities And Selenium In Elderly Subjects And In Dementia Of Alzheimer's Type-Place Of The Extracellular Glutathione Peroxidase," <i>Free Radic. Biol. Med.</i> 20:579-587, Elsevier Science (1996).

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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	<u>10</u>	Chan, C.-W., et al., "Anti-apoptotic action of Alzheimer A β ," <i>Alzheimer's Reports</i> 2:113-119, MSJ (March 1999).
AS	<u>10</u>	Cherny, R.A., et al., "The Aggregation of A β in Human Brain is Mediated by Zinc," <i>Soc. for Neurosci. Abstracts</i> 23:534, Society for Neuroscience (1997).
AT	<u>10</u>	Cherny, R.A., et al., "Aqueous Dissolution of Alzheimer's Disease A β Amyloid Deposits by Biometal Depletion," <i>J. Biol. Chem.</i> 274:23223-23228, American Society for Biochemistry and Molecular Biology (August 1999).

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		APPLICANT Bush et al.			
		FILING DATE August 19, 2003		GROUP 1614	

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AR	<u>11</u>	Chong, Y.-H., and Suh, Y.-H., "Aggregation of amyloid precursor proteins by aluminum in vitro," <i>Brain Res.</i> 670:137-141, Elsevier-North Holland Biomedical Press (1995).
AS	<u>11</u>	Cohen, A.S., "Amyloidosis," in <i>Arthritis and Allied Conditions- A Textbook of Rheumatology</i> , D.J. McCarty, ed., Lea and Febiger, Philadelphia, pp. 1273-1293 (1989).
AT	<u>11</u>	Colaco, C.A.L.S., et al., "The role of the Maillard reaction in other pathologies: Alzheimer's disease," <i>Nephrol. Dial. Transplant.</i> 11(Suppl. 5):7-12, Oxford University Press (1996).

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AR	<u>12</u>	Connor, J.R., et al., "A Histochemical Study of Iron, Transferrin, and Ferritin in Alzheimer's Diseased Brains," <i>J. Neurosci. Res.</i> 31:75-83, Society for Neuroscience (1992).
AS	<u>12</u>	Connor, J.R., et al., "Ceruloplasmin levels in the human superior temporal gyrus in aging and Alzheimer's disease," <i>Neurosci. Lett.</i> 159:88-90, Elsevier Scientific Publishers (1993).
AT	<u>12</u>	Coyle, J.T., and Puttfarcken, P., "Oxidative Stress, Glutamate, and Neurodegenerative Disorders," <i>Science</i> 262:689-695, American Association for the Advancement of Science (1993).

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AR	<u>13</u>	Crapper McLachlan, D.R., et al., "Intramuscular desferrioxamine in patients with Alzheimer's disease," Lancet 337:1304-1308, Lancet Publishing Group (1991).
AS	<u>13</u>	Cuajungco, M.P., and Lees, G.J., "Zinc and Alzheimer's disease: is there a direct link?" Brain Res. Rev. 23:219-236, Elsevier Science Publishers (April 1997).
AT	<u>13</u>	Dedman, D.J., et al., "Iron and aluminum in relation to brain ferritin in normal individuals and Alzheimer's-disease and chronic renal-dialysis patients," Biochem J. 287:509-514, Biochemical Society/Portland Press (1992).

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AR	<u>14</u>	Deibel, M.A., et al., "Copper, iron, and zinc imbalances in severely degenerated brain regions in Alzheimer's disease: possible relation to oxidative stress," <i>J. Neurol. Sci.</i> 143:137-142, Elsevier (November 1996).
AS	<u>14</u>	Doré, S., et al., "Insulin-like growth factor I protects and rescues hippocampal neurons against β-amyloid- and human amylin-induced toxicity," <i>Proc. Natl. Acad. Sci. USA</i> 94:4772-4777, National Academy of Sciences (April 1997).
AT	<u>14</u>	Dyrks, T., et al., "Amyloidogenicity of βA4 and βA4-bearing Amyloid Protein Precursor Fragments by Metal-catalyzed Oxidation," <i>J. Biol. Chem.</i> 267:18210-18217, American Society for Biochemistry and Molecular Biology (1992).

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AR	<u>15</u>	Ehmann, W.D., et al., "Brain Trace Elements in Alzheimer's Disease," NeuroToxicology 7:197-206, Pathotox Publishers (1986).
AS	<u>15</u>	Esler, W.P., et al., "Zinc-Induced Aggregation of Human and Rat β -Amyloid Peptides In Vitro," J. Neurochem. 66:723-732, Blackwell Science (February 1996).
AT	<u>15</u>	Esler, W.P., et al., "A β deposition inhibitor screen using synthetic amyloid," Nat. Biotechnol. 15:258-263, Nature Publishing Co. (March 1997).

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AR	<u>16</u>	Fitzgerald, D.J., "Zinc and Alzheimer's Disease," <i>Science</i> 268:1920, American Association for the Advancement of Science (1995).
AS	<u>16</u>	Folstein, M., "Nutrition and Alzheimer's Disease," <i>Nutrition Reviews</i> 55:23-25, International Life Sciences Institute (January 1997).
AT	<u>16</u>	Fraser, P.E., et al., "pH-dependent structural transitions of Alzheimer amyloid peptides," <i>Biophys. J.</i> 60:1190-1201, Rockefeller University Press (1991).

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AR	<u>17</u>	Frederikse, P.H., et al., "Oxidative Stress Increases Production of β -Amyloid Precursor Protein and β -Amyloid ($A\beta$) in Mammalian Lenses, and $A\beta$ Has Toxic Effects on Lens Epithelial Cells," <i>J. Biol. Chem.</i> 271:10169-10174, American Society for Biochemistry and Molecular Biology (April 1996).
AS	<u>17</u>	Frederickson, C.J., "Neurobiology of Zinc and Zinc-Containing Neurons," <i>Int. Rev. Neurobiol.</i> 31:145-238, Academic Press (1989).
AT	<u>17</u>	Frieden, E., "Ceruloplasmin: A Multi-functional Cupro-protein of Vertebrate Plasma," in: <i>Inflammatory Diseases and Copper</i> , Sorenson, J.R.J., ed., Clifton, N.J., Humana Press, pp.159-169 (1982).

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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	<u>18</u>	Garzon-Rodriguez, W., et al., "Soluble Amyloid A β -(1-40) Exists as a Stable Dimer at Low Concentrations," <i>J. Biol. Chem.</i> 272:21037-21044, American Society for Biochemistry and Molecular Biology (August 1997).
AS	<u>18</u>	Giampaolo, V., "Copper and Inflammation," in <i>Inflammatory Diseases and Copper</i> , Sorenson, J.R.J., ed., Clifton, N.J., Humana Press, pp. 329-345 (1982).
AT	<u>18</u>	Giulian, D., et al., "Specific Domains of β -Amyloid from Alzheimer Plaque Elicit Neuron Killing in Human Microglia," <i>J. Neurosci.</i> 16:6021-6037, Society for Neuroscience (October 1996).

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	<u>19</u>	Glenner, G.G., and Wong, C.W, "Alzheimer's Disease: Initial Report of the Purification and Characterization of Novel Cerebrovascular Amyloid Protein," <i>Biochem. Biophys. Res. Commun.</i> 120:885-890, Academic Press (1984).
AS	<u>19</u>	Golde, T.E., et al., "Processing of the Amyloid Protein Precursor to Potentially Amyloidogenic Derivatives," <i>Science</i> 255:728-730, American Association for the Advancement of Science (1992).
AT	<u>19</u>	Good, P.F., et al., "Selective Accumulation of Aluminum and Iron in the Neurofibrillary Tangles of Alzheimer's Disease: A Laser Microprobe (LAMMA) Study," <i>Ann. Neurol.</i> 31:286-292, Wiley-Liss (1992).

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	AR	<u>20</u>	Goodman, Y., et al., "Nordihydroguaiaretic acid protects hippocampal neurons against amyloid β -peptide toxicity, and attenuates free radical and calcium accumulation," <i>Brain Res.</i> 654:171-176, Elsevier/North-Holland Biomedical Press (1994).
	AS	<u>20</u>	Goodman, Y., and Mattson, M.P., "Secreted Forms of β -Amyloid Precursor Protein Protect Hippocampal Neurons against Amyloid β -Peptide-Induced Oxidative Injury," <i>Exp. Neurol.</i> 128:1-12, Academic Press (1994).
	AT	<u>20</u>	Gorevic, P.D., et al., "The Biological Significance of Amyloid," <i>Ann. New York Acad. Sci.</i> 389:380-394, New York Academy of Sciences (1982).

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AR	<u>21</u>	Goto, J.J., et al., "Reactions of Hydrogen Peroxide with Familial Amyotrophic Lateral Sclerosis Mutant Human Copper-Zinc Superoxide Dismutases Studied by Pulse Radiolysis," <i>J. Biol. Chem.</i> 273:30104-30109, American Association for the Advancement of Science (November 1998).
AS	<u>21</u>	Grundke-Iqbali, I., et al., "Ferritin is a component of the neuritic (senile) plaque in Alzheimer dementia," <i>Acta Neuropathol.</i> 81:105-110, Springer Verlag (1990).
AT	<u>21</u>	Gutteridge, J.M.C., and Wilkins, S., "Copper Salt-Dependent Hydroxyl Radical Formation Damage to Proteins Acting as Antioxidants," <i>Biochim. Biophys. Acta</i> 759:38-41, Academic Press (1983).

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AR	<u>22</u>	Haass, C., et al., "Amyloid β -peptide is produced by cultured cells during normal metabolism," <i>Nature</i> 359:322-325, Nature Publishing Co. (1992).
AS	<u>22</u>	Haley, J.V., "Zinc Sulfate and Wound Healing," <i>J. Surg. Res.</i> 27:168-174, Academic Press (1979).
AT	<u>22</u>	Halliwell, B., and Gutteridge, J.M.C., "Oxygen toxicity, oxygen radicals, transition metals and disease," <i>Biochem. J.</i> 219:1-14, Biochemical Society/Portland Press (1984).

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AR	<u>24</u>	Hansen, M.B., et al., "Re-examination and further development of a precise and rapid dye method for measuring cell growth/cell kill," <i>J. Immunol. Meth.</i> 119:203-210, North-Holland Pub. Co. (1989).
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AT	<u>24</u>	Harris, M.E., et al., "Direct Evidence of Oxidative Injury Produced by the Alzheimer's β -Amyloid Peptide (1-40) in Cultured Hippocampal Neurons," <i>Exp. Neurol.</i> 131:193-202, Academic Press (1995).

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	AL						Yes No
	AM						Yes No
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	AO						Yes No
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AR	<u>25</u>	Hensley, K., et al., "A model for beta-amyloid aggregation and neurotoxicity based on free radical generation by the peptide: Relevance to Alzheimer disease," Proc. Natl. Acad. Sci. USA 91:3270-3274, National Academy of Sciences (1994).
AS	<u>25</u>	Hensley, K., et al., "Brain Regional Correspondence Between Alzheimer's Disease Histopathology and Biomarkers of Protein Oxidation," J. Neurochem. 65:2146-2156, Blackwell Science (1995).
AT	<u>25</u>	Hensley, K., et al., "Reactive Oxygen Species as Causal Agents in the Neurotoxicity of the Alzheimer's Disease-Associated Amyloid Beta Peptide," Ann. N.Y. Acad. Sci. 786:120-134, New York Academy of Sciences (June 1996).

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		APPLICANT Bush et al.			
		FILING DATE August 19, 2003		GROUP 1614	

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	AR	26	Hesse, L., et al., "The β A4 amyloid precursor protein binding to copper," FEBS Lett. 349:109-116, Federation of European Biochemical Societies (1994).
.	AS	26	Hilbich, C., et al., "Aggregation and Secondary Structure of Synthetic Amyloid β A4 Peptides of Alzheimer's Disease," J. Mol. Biol. 218:149-163, Academic Press (1991).
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AR	<u>27</u>	Hsu, J.M., et al., "Zinc deficiency and incorporation of 14C-labeled methionine into tissue proteins in rats," <i>J. Nutr.</i> 99:425-432, American Institute of Nutrition (1969).
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AR	<u>28</u>	Ida, N., et al., "Analysis of Heterogeneous β A4 Peptides in Human Cerebrospinal Fluid and Blood by a Newly Developed Sensitive Western Blot Assay," <i>J. Biol. Chem.</i> 271:22908-22914, American Society for Biochemistry and Molecular Biology (September 1996).
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AR	<u>29</u>	Johnstone, E.M., et al., "Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis," <i>Mol. Brain Res.</i> 10:299-305, Elsevier Science Publishers (1991).
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AT	<u>29</u>	Kang, J., et al., "The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor," <i>Nature</i> 325:733-736, Nature Publishing Co. (1987).

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		FILING DATE August 19, 2003	GROUP 1614

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AT	<u>30</u>	Kidani, Y., et al., "Mass spectrometry of 5-chloro-7-iodo-8-quinolinol metal chelates," <i>Jpn. Analyst</i> 23:1375-1378, Nippon Bunseki Kagakka (1974).

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AR	<u>31</u>	Kirschner, D.A., et al., "Synthetic peptide homologous to β protein from Alzheimer disease forms amyloid-like fibrils in vitro," Proc. Natl. Acad. Sci. USA 84:6953-6957, National Academy of Sciences (1987).
AS	<u>31</u>	Kirshenbaum, K., and Daggett, V., "pH-Dependent Conformations of the Amyloid β (1-28) Peptide Fragment Explored Using Molecular Dynamics," Biochemistry 34:7629-7639, American Chemical Society (1995).
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AR	<u>32</u>	Kisilevsky, R., "Inflammation-Associated Amyloidogenesis," <i>Mol. Neurobiol.</i> 8:65-66, Humana Press (1994).
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AR	<u>33</u>	Kuo, Y.-M., et al., "High Levels of Circulating A β 42 Are Sequestered by Plasma Proteins in Alzheimer's Disease," <i>Biochem. Biophys. Res. Commun.</i> 257:787-791, Academic Press (April 1999).
AS	<u>33</u>	Kuo, Y.-M., et al., "Water-soluble A β (N-40, N-42) Oligomers in Normal and Alzheimer Disease Brains," <i>J. Biol. Chem.</i> 271:4077-4081, American Society of Biochemistry and Molecular Biology (February 1996).
AT	<u>33</u>	Landers, J.W., and Zak, B., "Determination of Serum Copper and Iron in a Single Small Sample," <i>Am. J. Clin. Pathol.</i> 29:590-592, American Society of Clinical Pathologists (1958).

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AR	<u>34</u>	Lindeman, R.D., et al., "Myocardial zinc metabolism in experimental myocardial infarction," <i>J. Lab. Clin. Med.</i> 81:194-204, Mosby-Year Book (1973).
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AT	<u>34</u>	Lockhart, B.P., et al., "Inhibitors of free radical formation fail to attenuate direct beta-amyloid ₂₅₋₃₅ peptide-mediated neurotoxicity in rat hippocampal cultures," <i>J. Neurosci. Res.</i> 39:494-505, Wiley Interscience (1994).

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AR	<u>35</u>	Lohr, J.B., "Oxygen Radicals and Neuropsychiatric Illness," Arch. Gen. Psychiatry 48:1097-1106, American Medical Association (1991).
AS	<u>35</u>	Lovell, M.A., et al., "Copper, iron and zinc in Alzheimer's disease senile plaques," J. Neurol. Sci. 158:47-52, Elsevier (June 1998).
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AT	<u>36</u>	Markesberry, W.R., "Oxidative Stress Hypothesis in Alzheimer's Disease," <i>Free Rad. Biol. Med.</i> 23:134-147, Elsevier Science (1997).

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AT	<u>38</u>	Mecocci, P., et al., "Oxidative Damage to Mitochondrial DNA Shows Marked Age-dependent Increases in Human Brain," <i>Ann. Neurol.</i> 34:609-616, Wiley-Liss (1993).

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		APPLICANT Bush et al.	
		FILING DATE August 19, 2003	GROUP 1614

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	AL						Yes No
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AR	40	Moir, R.D., et al., "Relative Increase in Alzheimer's Disease of Soluble Forms of Cerebral A β Amyloid Protein Precursor Containing the Kunitz Protease Inhibitory Domain," <i>J. Biol. Chem.</i> 273:5013-5019, American Society for Biochemistry and Molecular Biology (February 1998).
AS	40	Mok, S.S., et al., "A Novel Metalloprotease in Rat Brain Cleaves the Amyloid Precursor Protein of Alzheimer's Disease Generating Amyloidogenic Fragments," <i>Biochemistry</i> 36:156-163, American Chemical Society (January 1997).
AT	40	Kang, J., et al., "The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor," <i>Nature</i> 325:733-736, Nature Publishing Co. (1987).

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AR	<u>41</u>	Multhaup, G., et al., "Interaction between the zinc(II) and the heparin binding site of the Alzheimer's disease β A4 amyloid precursor protein (APP)," FEBS Lett. 355:151-154, Federation of European Biochemical Societies (1994).
AS	<u>41</u>	Multhaup, G., et al., "The Amyloid Precursor Protein of Alzheimer's Disease in the Reduction of Copper(II) to Copper(I)," Science 271:1406-1409, American Association for the Advancement of Science (March 1996).
AT	<u>41</u>	Munch, G., et al., "Advanced glycation endproducts in ageing and Alzheimer's disease," Brain Res. Rev. 23:134-143, Elsevier Science B.V. (February 1997).

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AR	<u>42</u>	Nakada, T., and Kwee, I.L., "Guanidinoethane sulfate: brain pH alkaline shifter," <i>NeuroReport</i> 4:1035-1038, Lippincott Williams & Wilkins (1993).
AS	<u>42</u>	Nunomura, A., et al., "RNA Oxidation Is a Prominent Feature of Vulnerable Neurons in Alzheimer's Disease," <i>J. Neurosci.</i> 19:1959-1964, Society for Neuroscience (March 1999).
AT	<u>42</u>	Okada, H., et al., "Effects of Metal-Containing Drugs Taken Simultaneously with Clioquinol Upon Clinical Features of SMON," <i>J. Toxicol. Sci.</i> 9:327-341, Doku Say o Kenky ukai (1984).

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AR	<u>43</u>	Owen, C.A., Jr., "Uptake of ⁶⁷ Cu by Ceruloplasmin In Vitro (38878)," Proc. Soc. Exp. Biol. Med. 149:681-682, Blackwell Science (1975).
AS	<u>43</u>	Padmanabhan, G., et al., "Clioquinol," in <i>Analytical Profiles of Drug Substances</i> , Volume 18, Florey, K., ed., Academic Press, Inc., San Diego, CA, pp. 57-90 (1989).
AT	<u>43</u>	Pepys, M.B., and Baltz, M.L., "Acute Phase Proteins with Special Reference to C-Reactive Protein and Related Proteins (Pentaxins) and Serum Amyloid A Protein," in <i>Advances in Immunology</i> , Vol. 34, pp.141-212, Academic Press (1983).

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AR	<u>44</u>	Pérez, A.A., et al., "Alzheimer Amyloids A β 1-40 and A β 1-42 are Differentially Degraded by Insulin Degrading Enzyme (IDE) From Human Brain," <i>Soc. Neurosci. Abstracts</i> 23:821, Society for Neuroscience (1997).
AS	<u>44</u>	Peters, G., and Rodgers, M.A.J., "Single-Electron Transfer from NADH Analogues to Singlet Oxygen," <i>Biochim. Biophys. Acta</i> 637:43-52, Elsevier (1981).
AT	<u>44</u>	Pierce, J.E.S., et al., "Immunohistochemical Characterization of Alterations in the Distribution of Amyloid Precursor Proteins and β -Amyloid Peptide after Experimental Brain Injury in the Rat," <i>J. Neurosci.</i> 16:1083-1090, Society for Neuroscience (February 1996).

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AR	<u>45</u>	Potempa, L.A., et al., "Effect of Divalent Metal Ions and pH upon the Binding Reactivity of Human Serum Amyloid P Component, a C-reactive Protein Homologue, for Zymosan," <i>J. Biol. Chem.</i> 260:12142-12147, American Society for Biochemistry and Molecular Biology (1985).
AS	<u>45</u>	Raby, C.A., et al., "Traumatic Brain Injury Increases β -Amyloid Peptide 1-42 in Cerebrospinal Fluid," <i>J. Neurochem.</i> 71:2505-2509, Blackwell Science (December 1998).
AT	<u>45</u>	Richardson, J.S., et al., "On the Possible Role of Iron-Induced Free Radical Peroxidation in Neural Degeneration in Alzheimer's Disease," <i>Ann. N.Y. Acad. Sci.</i> 648:326-327, New York Academy of Sciences (1992).

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AR	<u>46</u>	Roberts, G.W., et al., "βA4 amyloid protein deposition in brain after head trauma," <i>Lancet</i> 338:1422-1423, Lancet Press (1991).
AS	<u>46</u>	Robinson, S.R., et al., "Most amyloid plaques contain ferritin-rich cells," <i>Alzheimer's Res.</i> 1:191-196, Rapid Science Publishers (1995).
AT	<u>46</u>	Rogers, J., et al., "Clinical trial of indomethacin in Alzheimer's disease," <i>Neurology</i> 43:1609-1611, Lippincott, Williams & Wilkins (1993).

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AR	<u>47</u>	Roher, A.E., et al., "Morphology and Toxicity of A β -(1-42) Dimer Derived from Neuritic and Vascular Amyloid Deposits of Alzheimer's Disease," <i>J. Biol. Chem.</i> 271:20631-20635, American Society for Biochemistry and Molecular Biology (August 1996).
AS	<u>47</u>	Rosen, D., et al., "Mutations in Cu/Zn superoxide dismutase gene are associated with familial amyotrophic lateral sclerosis," <i>Nature</i> 362:59-62, Nature Publishing Co. (1993).
AT	<u>47</u>	Rumble, B., et al., "Amyloid A4 Protein and Its Precursor in Down's Syndrome and Alzheimer's Disease," <i>New Eng. J. Med.</i> 320:1446-1452, Massachusetts Medical Society (1989).

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AR	<u>48</u>	Sadowski, M., et al., "Astrocyte and microglia reaction in Alzheimer's disease in the hippocampal formation- a quantitative analysis," <i>Alzheimer's Res.</i> 1:71-76, Rapid Science Publishers (1995).
AS	<u>48</u>	Sano, M., et al., "A Controlled Trial of Selegiline, Alpha-Tocopherol, or Both as Treatment for Alzheimer's Disease," <i>N. Engl. J. Med.</i> 336:1216-1222, Massachusetts Medical Society (April 1997).
AT	<u>48</u>	Sayre, L.M., "Alzheimer's Precursor Protein and the Use of Bathocuproine for Determining Reduction of Copper(II)," <i>Science</i> 274:1933-1934, American Association for the Advancement of Science (December 1996).

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AR	<u>49</u>	Schnabel, J., "New Alzheimer's Therapy Suggested," <i>Science</i> 260:1719-1720, American Association for the Advancement of Science (1993).
AS	<u>49</u>	Schrader-Fischer, G., and Pagnetto, P.A., "Effect of alkalinizing agents on the process of the β -amyloid precursor protein," <i>Brain Res.</i> 716:91-100, Elsevier/North-Holland Biomedical Press (April 1996).
AT	<u>49</u>	Schubert, D., and Chevion, M., "The Role of Iron in Beta Amyloid Toxicity," <i>Biochem. Biophys. Res. Commun.</i> 216:702-707, Academic Press (1995).

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AR	<u>50</u>	Selkoe, D.J., "Cell Biology of the Amyloid β -protein Precursor and the Mechanism of Alzheimer's Disease," <i>Ann. Rev. Cell Biol.</i> 10:373-403, Annual Reviews, Inc. (1994).
AS	<u>50</u>	Seubert, P., et al., "Isolation and quantification of soluble Alzheimer's β -peptide from biological fluids," <i>Nature</i> 359:325-327, Nature Publishing Co. (1992).
AT	<u>50</u>	Shiraki, H., "Neuropathological aspects of the etiopathogenesis of subacute myelo-optico-neuropathy (SMON)," in <i>Handbook of Clinical Neurology. Intoxications of the Nervous System Part II</i> , Vinken, P.J., and Bruyn, G.W., eds., North-Holland Publishing Company, Amsterdam, Holland, pp.141-198 (1979).

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AR	<u>51</u>	Shivers, B.D., et al., "Alzheimer's disease amyloidogenic glycoprotein: expression pattern in rat brain suggests a role in cell contact," <i>EMBO J.</i> 7:1365-1370, European Molecular Biology Organization (1988).
AS	<u>51</u>	Shoji, M., et al., "Production of the Alzheimer Amyloid β Protein by Normal Proteolytic Processing," <i>Science</i> 258:126-129, American Association for the Advancement of Science (1992).
AT	<u>51</u>	Sisodia, S.S., et al., "Cellular and molecular biology of Alzheimer's disease and animal models," <i>Neurodegenerative Diseases</i> 5:59-68, Karger (1995).

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AR	<u>52</u>	Skinner, M., et al., "Observations on the amyloid-degrading activity of serum and its relationship to human neutrophil elastase," <i>Trans. Assoc. Am. Phys.</i> 96:437-443, William J. Dornan (1983).
AS	<u>52</u>	Smalheiser, N.R., and Swanson, D.R., "Indomethacin and Alzheimer's disease," <i>Neurology</i> 46:583, Lippincott, Williams & Wilkins (February 1996).
AT	<u>52</u>	Smith, C., et al., "The molecular pathology of Alzheimer's disease: are we any closer to understanding the neurodegenerative process?" <i>Neuropathol. Appl. Neurobiol.</i> 20:322-338, Blackwell Scientific Publications (1994).
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AR	<u>53</u>	Smith, M.A., et al., "Radical Ageing in Alzheimer's disease," <i>Trends Neurosci.</i> 18:172-176, Elsevier Applied Science Publishing (1995).
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AT	<u>53</u>	Smith, M.A., et al., "Iron accumulation in Alzheimer disease is a source of redox-generated free radicals," <i>Proc. Natl. Acad. Sci. USA</i> 94:9866-9868, National Academy of Sciences (September 1997).

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	AR	<u>54</u>	Sobue, I., "Clinical aspects of subacute myelo-optico-neuropathy (SMON)," in <i>Handbook of Clinical Neurology. Intoxications of the Nervous System Part II</i> , Vinken, P.J., and Bruyn, G.W., eds., North-Holland Publishing Company, Amsterdam, Holland, pp.115-139 (1979).
	AS	<u>54</u>	Soto, C., et al., " β -sheet breaker peptides inhibit fibrillogenesis in a rat brain model of amyloidosis: Implications for Alzheimer's therapy," <i>Nature Med.</i> 4:822-826, Nature Publishing Co. (July 1998).
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		APPLICANT Bush et al.			
		FILING DATE August 19, 2003		GROUP 1614	

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AS	<u>55</u>	Stankovic, A., and Mitrovic, D.R., "Aluminum Salts Stimulate Luminol-Enhanced Chemiluminescence Production by Human Neutrophils," <i>Free Rad. Res. Commun.</i> 14:47-55, Harwood Academic Publishers (1991).
AT	<u>55</u>	Suzuki, N., et al., "An Increased Percentage of Long Amyloid β -Protein Secreted by Familial Amyloid β -Protein Precursor (β APP ₇₁) Mutants," <i>Science</i> 264:1336-1340, American Association for the Advancement of Science (1994).

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AS	<u>56</u>	Tanzi, R.E., et al., "Amyloid β Protein Gene: cDNA, mRNA Distribution, and Genetic Linkage Near the Alzheimer Locus," <i>Science</i> 235:880-884, American Association for the Advancement of Science (1987).
AT	<u>56</u>	Tamura, Z., "Clinical Chemistry of Clioquinol," <i>Jpn. J. Med. Sci. Biol.</i> 28:69-77, Kokuritsu Yobo Eisei Kenkyujo (1975).

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AS	<u>57</u>	Tateishi, J., et al., "Myeloneuropathy in dogs induced by iodoxyquinoline," <i>Neurology</i> 22:702-709, Lippincott, Williams & Wilkins (1972).
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AR	<u>59</u>	Teller, J.K., et al., "Presence of soluble amyloid β -peptide precedes amyloid plaque formation in Down's Syndrome," <i>Nature Med.</i> 2:93-95, Nature Publishing Co. (January 1996).
AS	<u>59</u>	Terhune, M.W., and Sandstead, H.H., "Decreased RNA Polymerase Activity in Mammalian Zinc Deficiency," <i>Science</i> 177:68-69, American Association for the Advancement of Science (1972).
AT	<u>59</u>	Terry, R.D., et al., "Physical Basis of Cognitive Alterations in Alzheimer's Disease: Synapse Loss Is the Major Correlate of Cognitive Impairment," <i>Ann. Neurol.</i> 30:572-580, Wiley-Liss (1991).

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			APPLICANT Bush et al.			
			FILING DATE August 19, 2003		GROUP 1614	

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	AR	<u>61</u>	Thompson, C.M., et al., "Regional Brain Trace-Element Studies in Alzheimer's Disease," NeuroToxicol. 9:1-7, Pathotox Publishers (1988).
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	AR	<u>62</u>	Uchida, K., and Kawakishi, S., "Identification of Oxidized Histidine Generated at the Active Site of Cu,Zn-Superoxide Dismutase Exposed to H ₂ O ₂ . Selective Generation Of 2-Oxo-Histidine At The Histidine 118," J. Biol. Chem. 269:2405-2410, American Society for Biochemistry and Molecular Biology (1994).				
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	AT	<u>62</u>	Warren, P.J., et al., "The Distribution of Copper in Human Brain," Brain 83:709-717, Oxford University Press (1960).				
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AR	<u>63</u>	Weismann, K., and Knudsen, L., "Effects of Penicillamine and Hydroxyquinoline on Absorption of Orally Ingested ⁶⁵ Zinc in the Rat," <i>J. Invest. Dermatol.</i> 71:242-244, Blackwell Science (1978).
AS	<u>63</u>	Wolozin, B., et al., "Participation of presenilin 2 in Apoptosis: Enhanced Basal Activity Conferred by an Alzheimer Mutation," <i>Science</i> 274:1710-1713, American Association for the Advancement of Science (December 1996).
AT	<u>63</u>	Wood, S.J., et al., "Physical, Morphological and Functional Differences between pH 5.8 and 7.4 Aggregates of the Alzheimer's Amyloid Peptide A β ," <i>J. Mol. Biol.</i> 256:870-877, Academic Press (March 1996).

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	AR	<u>64</u>	Yankner, B.A., et al., "Neurotrophic and Neurotoxic Effects of Amyloid β Protein: Reversal by Tachykinin Neuropeptides," <i>Science</i> 250:279-282, American Association for the Advancement of Science (1990).
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AT	<u>68</u>	Van Reyk, D.M., and Dean, R.T., "The Iron-selective Chelator Desferal Can Reduce Chelated Copper," <i>Free Rad. Res.</i> 24:55-60, Harwood Academic Publishers GmbH (January 1996).

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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>			ATTY. DOCKET NO. 0609.4810002/TJS/FRC	APPLICATION NO. 10/643,226
			APPLICANT Bush et al.	
			FILING DATE August 19, 2003	GROUP 1614

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
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	AK						

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP			.			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	69	Dialog File 351, Accession Number 8749401, Derwent WPI English language abstract for DE 40 04 978 A1 (Document AL4).
	AS	69	Behl, C., et al., "Hydrogen Peroxide Mediates Amyloid β Protein Toxicity," Cell 77:817-827, Cell Press (1994).
	AT	69	Walter, M.F., et al., "Alzheimer's Disease Amyloid β Peptide 25-35 Inhibits Lipid Peroxidation as a Result of Its Membrane Interactions," Biochem. Biophys. Res. Commun. 233:760-764, Academic Press (April 1997).

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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	<u>70</u>	Aisen, P.S., et al., "Randomized pilot study of nimesulide treatment in Alzheimer's disease," <i>Neurology</i> 58:1050-1054, AAN Enterprises, Inc. (April 2002).
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AT		

EXAMINER	DATE CONSIDERED
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